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10/551,667	07/18/2006	Patrick Y Lu	INTM/017	5623

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EXAMINER	
VIVLEMORE, TRACY ANN	
ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,667	LU ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33,35-43,51,52,57-67,70 and 73-85* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *70,73 and 76* is/are allowed.

6)☒ Claim(s) *33,35-43,51,52,57,58,66,67,74,77-83 and 85* is/are rejected.

7)☒ Claim(s) *59-65,75 and 84* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 October 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection or objection not reiterated in this Action is withdrawn.

Status of the application

In the reply filed October 29, 2008, new claims 77-85 have been added. Claims 33, 35-43, 51, 52, 57-67, 70 and 73-85 are pending and under examination.

Claim Objections

Claim 84 is objected to because of the following informalities: this claim is directed to a nucleic acid that is complementary to SEQ ID NO: 21 or 22, indicating that these are target sequences, however page 60 of the specification states that SEQ ID NOs: 21 and 22 are "siRNAs targeting the sense strand of mRNA". Since the specification discloses that these sequences target the sense strand, it indicates that SEQ ID NOs: 21 and 22 are themselves the antisense sequence. Clarification is requested whether the recited sequences are antisense sequences or target sequences.

Claim Rejections - 35 USC § 112

Claim 85 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention. Claim 85 recites the limitation "the antisense nucleic acid of claim 81" in line 2. There is insufficient antecedent basis for this limitation in the claim because claim 81 does not recite a nucleic acid. For the purposes of examination this claim is interpreted as depending from claim 84.

Claim 77 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

This claim recites the limitation that the cancer being treated is breast, melanoma or head and neck cancer. Applicants point to pages 18, 31 and 36 as providing support for this claim, however these pages provide support only for breast cancer. Treatment of melanoma is not contemplated at all and the only support for head and neck cancer is the contemplation of parotid gland cancer. While this is one type of cancer that falls under the broader category of head and neck cancer it does not by itself provide support for this broader category.

Claims 33, 35, 43, 51, 52, 57, 58, 77 and 79-83 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are directed to methods of inhibiting ICT1024 expression by administering an inhibitor of ICT1024 polypeptide, DNA or RNA that inhibits ICT1024 expression or activity. In specific embodiments the method is performed for the purpose of treating cancer, increasing apoptosis, reducing proliferation or reducing growth of a tumor.

The gene designated by applicants as ICT1024 is EGFR-RP, epithelial growth factor receptor-related protein. The specification teaches that EGF-RP shares homology with multiple cDNA sequences, each of which encode the same 855 amino acid protein and that the biological activity of this protein is unknown. The specification discloses at pages 38-39 that the inhibitors useful in the claimed methods include nucleic acid based inhibitors such as antisense, ribozymes and siRNAs and other, non-nucleic acid inhibitors such as protein antagonist, small molecule inhibitors and "other types of inhibitors". The specification exemplifies the use of siRNAs targeted to ICT1024 and those of skill in the art are aware that nucleic acid based inhibitors can be designed for any gene whose sequence is known.

The claimed methods embrace the use of inhibitors such as protein antagonists and small molecules. The specification does not describe any non-nucleic acid inhibitors of ICT1024, and the prior art also fails to describe non-nucleic acid inhibitors of ICT1024 that specifically reduce activity of ICT1024 polypeptide.

In order for the written description provision of 35 USC 112, first paragraph to be satisfied, applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed. For example, MPEP 2163 states in part,

> "An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.")."

The skilled artisan cannot envision the detailed structure of the full genus of the encompassed inhibitors of ICT1024, particularly non-nucleic acid inhibitors, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention.

Therefore, the full breadth of ICT1024 inhibitors encompassed by the claims do not meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant.

Claims 33, 35-43, 51, 52, 66, 67, 74 and 77-83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing breast cancer growth, increasing apoptosis and reducing proliferation of breast cancer cells,

does not reasonably provide enablement for reducing precancerous growths of any type or for reducing growth or proliferation of other cancers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors as enumerated *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), are considered when making a determination that a disclosure is not enabling: the breadth of the claims, the nature of the invention, the state of the prior art, the level of ordinary skill in the art, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples and the quantity of experimentation needed to make the invention based on the content of the disclosure.

The claims are directed to reduction of cancer or precancerous growth in mammalian tissue, increasing apoptosis, reducing proliferation, or reducing growth of an ICT1024-expressing tumor by administering an inhibitor of ICT1024 expression. The inhibitor can be a variety of molecules such as antisense, siRNAs or decoys or can be non-nucleic acid inhibitors that decrease ICT1024 polypeptide activity. The claims further embrace treatment of numerous types of cancers.

The gene designated by applicants as ICT1024 is EGFR-RP, epithelial growth factor receptor-related protein, also referred to as human Rhomboid family-1, or RHBDF-1. The specification teaches that this gene shares homology with multiple cDNA sequences, each of which encode the same 855 amino acid protein and that the biological activity of this protein is unknown. The prior art does not disclose inhibition of

this gene to treat cancer, therefore any disclosure of this gene's association with treatment of cancer or precancerous growths is limited to that found within the instant specification.

The specification discloses that intratumoral administration of siRNAs targeted to ICT1024 decreased breast cancer tumor xenografts in a mouse model. The specification further discloses that expression profiling shows that ICT1024 is upregulated in other cancerous tissues but does not demonstrate that other types of cancers or precancerous growths of any type are reduced by any type of ICT1024 inhibitory molecule.

Because of the lack of guidance in the specification and in the prior art demonstrating an effect of inhibiting ICT1024 in cancers other than breast cancer and in any type of precancerous growth, the claims are not enabled throughout their full scope. Even several years post-filing this gene is not recognized as being a therapeutic target for cancers other than breast. See Yan et al. (Molecular Cancer Therapeutics 2008), who in the introduction characterize RHBDF-1 as a target for breast and head and neck cancers and "possibly other epithelial cell cancers". The discussion of this reference (pages 1362-1363) notes RHBDF-1 was readily detectable in a variety of breast cancer and head and neck cancer cell lines, and that this indicates that this gene may be active in cancer cells in general. While Yan et al. teaches that this gene is a plausible target for treatment of epithelial cancers, the speculative language used indicates that even in 2008 the connection between RHBDF-1 and most cancers is correlative, not causative.

Thus, while the specification is enabling for treatment of breast cancer, the specification is not enabling for the broad claims of reducing the growth or proliferation or increasing apoptosis of any other type of cancer or reducing the growth of any type of precancerous growth because a causative link has not been shown between ICT1024 expression and growth and/or proliferation of cancers other than breast. The amount of experimentation required is such that one of skill in the art could not practice the invention commensurate in scope with the claims without undue, trial and error experimentation and therefore, claims 33, 35-43, 51, 52, 66, 67, 74 and 77-83 are not enabled.

Response to Arguments

Applicants traverse the scope of enablement rejection by referring to the Yan et al. reference as demonstrating successful systemic administration of ICT1024 siRNAs using a delivery system contemplated by the instant specification. This argument is persuasive and the aspect of the enablement rejection relating to delivery of siRNA therapeutics is withdrawn, however the aspect relating to the treatment of other types of cancers remains as described in the revised rejection.

Allowable Subject Matter

SEQ ID NOs: 21 and 22 are free of the prior art searched, therefore claim 84 is considered to contain allowable subject matter pending clarification whether these

sequences are a target sequence or an antisense sequence. If claim 85 is meant to depend from claim 84 it would also be considered allowable upon amendment.

Claims 59-65 and 75 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 70, 73 and 76 are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is (571)272-2914. The examiner can normally be reached on Mon-Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz, can be reached on 571-272-0763. The central FAX Number is 571-273-8300.

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